

Amendments to the Specification:

Please replace the paragraph beginning at page 6, line 27, and continuing through page 7, line 14, with the following replacement paragraph:

The IFN- $\beta$  variants encompassed herein include muteins of the native mature IFN- $\beta$  sequence shown in SEQ ID NO:1 (see, for example, U.S. Patent No. 5,814,485, herein incorporated by reference), wherein one or more cysteine residues that are not essential to biological activity have been deliberately deleted or replaced with other amino acids to eliminate sites for either intermolecular crosslinking or incorrect intramolecular disulfide bond formation. IFN- $\beta$  variants of this type include those containing a glycine, valine, alanine, leucine, isoleucine, tyrosine, phenylalanine, histidine, tryptophan, serine, threonine, or methionine substituted for the cysteine found at amino acid 17 of the mature native amino acid sequence. Serine and threonine are the more preferred replacements because of their chemical analogy to cysteine. Serine substitutions are most preferred. See, for example, the IFN- $\beta$  variant where the cysteine found at amino acid 17 of the mature native sequence is replaced with serine (SEQ ID NO:2; U.S. Patent No. 5,814,485). Cysteine 17 may also be deleted using methods known in the art (see, for example, U.S. Patent No. 4,518,584, herein incorporated by reference), resulting in a mature IFN- $\beta$  mutein that is one amino acid shorter than the native mature IFN- $\beta$ . See also, as examples, U.S. Patent Nos. 4,530,787; 4,572,798; and 4,588,585. Thus, IFN- $\beta$  variants with one or more mutations that improve, for example, their pharmaceutical utility are also encompassed by the present invention.

Please replace the paragraph at page 9, line 1-24, with the following replacement paragraph:

Thus, the determination of percent identity between any two sequences can be accomplished using a mathematical algorithm. One preferred, non-limiting example of a mathematical algorithm utilized for the comparison of sequences is the algorithm of Myers and Miller (1988) *Comput. Appl. Biosci.* 4:11-7. Such an algorithm is utilized in the ALIGN program

(version 2.0), which is part of the GCG alignment software package. A PAM120 weight residue table, a gap length penalty of 12, and a gap penalty ~~[[or]]~~of 4 can be used with the ALIGN program when comparing amino acid sequences. Another preferred, non-limiting example of a mathematical algorithm for use in comparing two sequences is the algorithm of Karlin and Altschul (1990) *Proc. Natl. Acad. Sci. USA* 90:5873-5877, modified as in Karlin and Altschul (1993) *Proc. Natl. Acad. Sci. USA* 90:5873-5877. Such an algorithm is incorporated into the NBLAST and XBLAST programs of Altschul *et al.* (1990) *J. Mol. Biol.* 215:403-410. BLAST amino acid sequence searches can be performed with the XBLAST program, score = 50, wordlength = 3, to obtain amino acid sequence similar to the polypeptide of interest. To obtain gapped alignments for comparison purposes, gapped BLAST can be utilized as described in Altschul *et al.* (1997) *Nucleic Acids Res.* 25:3389-3402. Alternatively, PSI-BLAST can be used to perform an integrated search that detects distant relationships between molecules. See Altschul *et al.* (1997) *supra*. When utilizing BLAST, gapped BLAST, or PSI-BLAST programs, the default parameters can be used. See the website for [ncbi.nlm.nih.gov](http://ncbi.nlm.nih.gov). Also see the ALIGN program (Dayhoff (1978) in *Atlas of Protein Sequence and Structure* 5:Suppl. 3, National Biomedical Research Foundation, Washington, D.C.) and programs in the Wisconsin Sequence Analysis Package, Version 8 (available from Genetics Computer Group, Madison, Wisconsin), for example, the GAP program, where default parameters of the programs are utilized.